

To Mr. Bryant F.R.C.S. 7
With kindest regards
F. S. Dennis.

RECURRENCE.

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N. Y. City.

OF

CARCINOMA OF THE BREAST

BY

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RECURRENCE OF CARCINOMA OF THE BREAST.

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IN a study of the cases of recurrent carcinoma of the breast, only those will be considered in which a thorough microscopical examination of the tumor has been made. All other cases will be excluded as worthless, because a large number of benign as well as malignant tumors of the breast have been grouped under the general class of carcinoma. For these reasons as well as from the absence of a scientific diagnosis of the many different tumors affecting the breast, our knowledge of the recurrence of carcinoma in this organ is vague and untrustworthy. An attempt will be made to collect cases of recurrent carcinoma, utilizing only those, however, about which an authoritative statement can be made.

The points at issue in this paper are not the *relative frequency* of carcinoma of the breast or the *proportion* in which this disease exists in the sexes, or the *conditions* under which this neoplasm primarily develops, or the *etiology* of the growth. In other words, all the various subjects connected with carcinoma of the breast and collateral with it are not included in our discussion to-day. The title of our paper restricts us to one of the multifarious subjects incident to this disease. Any information upon the circumscribed limits of this single question may be regarded as a scientific contribution. Possibly many of us may live to see the day when the bacteriological origin of carcinoma will

be established, and it is to be hoped that this great discovery will be accompanied by an infallible remedy.

This knowledge, however, has not yet come, but the time has already arrived when an inquiry into the question of recurrence after surgical removal is pertinent.

The length of time that a patient may enjoy immunity from this disease after removal of the breast is a problem of overwhelming interest not only to the sufferer, but also to the surgeon.

The necessity of an investigation of carcinoma of the breast can be estimated when it is considered that in England alone there are 7000 deaths annually from carcinoma, and that there are 30,000 patients suffering at all times in that country from this affection, of which number a large proportion involve the breast. When it is considered that 50 per cent. of the cases of carcinoma of the breast die within three years, and that one-third die within two years, and that of all the tumors affecting the breast 80 per cent. consist of carcinoma, some idea can be formed of the overwhelming interest and paramount importance of our theme to-day.

The mere fact that carcinoma causes more deaths in the United States in one year than the sum-total of deaths due to erysipelas, tetanus, hydrophobia, lightning, typhlitis, gunshot wounds, joint disease, together with other well-known surgical affections, conveys at once an idea of the wide dimensions of our subject. When we learn that carcinoma causes nearly half as many deaths in one year in the United States as are caused by accidents and injuries of all kinds and descriptions, the importance of our subject is imperatively forced upon us.

Dr. Billings has demonstrated by statistics that carcinoma is a disease which is slowly increasing, and that it is the cause of a larger proportion of deaths in nations which have reached the highest state of civilization. For example, in the United States in one year there were over 13,000 deaths from carcinoma, of which there were twice as many deaths among females as among males. There are over 14,000 people in the United States dying each year from carcinoma. There were 1387

cases of death from carcinoma of the breast alone in this country during the year 1880.

It is evident, therefore, from these facts, that the question propounded for discussion is one calculated to awaken great interest.

As another instance of the necessity of investigating this subject may be cited the antagonistic views held by surgeons upon the question of curability or recurrence of carcinoma of the breast. Some surgeons have stated that breast carcinoma will always be found recurrent. In broad and striking contrast to this statement, other surgeons have expressed their opinions in favor of permanent cure of the disease after operation. With this wide diversity of opinion it is extremely opportune that the attention of this learned body should be directed to the solution of this intricate problem.

In order to facilitate the discussion of the subject of recurrence of carcinoma of the breast, it is necessary to collect the entire group of cases and then to deduct those cases from the whole number in which there has been a recurrence. This will furnish us with an approximate estimate of the number of cases in which a return of carcinoma occurs. I have carefully collected the compilation of cases supplied by the different writers upon carcinoma of the breast, and the result of my work demonstrates the fact that for our purpose a fairly uniform agreement is found as to the relative frequency of return of carcinoma of the breast after surgical interference. The cases of recurrence amount to about 75 per cent. of those collected. I have not included my own cases in this list because I shall take them up subsequently as a separate class and subject each case to a critical analysis in the light of the clinical history of the patient and the anatomical character of the tumor. The 75 per cent. of recurrences is high, but it represents approximately the general average if all the cases are taken into consideration.

These figures include cases where incomplete operations have been performed, that is to say, where the axilla has not been laid open and the chain of lymphatics removed whether they are diseased or not. If, however, only the cases in which a

complete operation has been performed, and only those of recent date, be considered, the percentage of returns would be much less, but the mortality of the operation correspondingly high. At all events, 75 per cent. of recurrences represent the aggregate collection of all cases by all writers up to the present time without including my own cases, and it is with this large number that the question propounded in the title of this paper is concerned.

To-day we have nothing to do with the 25 per cent. ending in permanent recovery. The fact that one-fourth of the cases never recur, points logically to the conclusion that in the other three-fourths of the cases there is either some defect in the operative technique, or there is an unreasonable delay in arriving at a positive diagnosis, or there is a great diversity in the histological formation of the carcinoma.

It is to an inquiry into the causes of recurrence in the 75 per cent. of the cases of carcinoma of the breast following excision of the gland that the attention of this Association is now directed.

From a very careful study of the cases of recurrence of carcinoma of the breast following excision of the gland, there is nothing in the recurrence of breast carcinoma different to what is found in the disease affecting other organs or parts. In our present state of knowledge all that can be said is that carcinoma develops in certain individuals who must have certain capabilities for the conception of the disease, and that the disease originates from some cause which excites cell-growth. In the primary growth at the beginning, the neoplasm is of local origin. Early and complete removal of the growth relieves the local disease; but the operation does not remove the predisposition or susceptibility or the capability for the recurrence of the disease. It is possible that the capability is limited to a certain extent, but to what extent no one can judge from a study of the life history of the growth.

One of the most striking illustrations of this fact occurred in the case of a lady who was a patient of Dr. Wm. Pierson, of Orange, N. J. This patient had a carcinoma of the breast

removed in 1855 by Dr. Hosack, and* the tumor was examined by the late Prof. Alonzo Clark, whose knowledge of the technique of the microscope no one would question. Over a third of a century after the removal of the breast the patient suffered from epithelioma of the rectum, from which disease she died. Here is a case in which there is no doubt as to the date of the operation and in which there is no question as to the character of the tumor, and thirty-six years elapsed without a return. I do not believe in this case that the epithelioma of the rectum had any relation to the carcinoma of the breast, and I do believe the operation cured the patient of breast carcinoma; but it did not cure the susceptibility or the predisposition. This is a valuable case for reference, because the microscopical examination was made at the time of the operation and at a period in the history of medicine when the microscope had not been employed to any extent for such purposes.

The many years from the date of the operation during which no return took place the patient was cured of carcinoma of the breast. The capability, however, was not removed by the operation. The operation, however, cured the carcinoma locally, and this case teaches us an important lesson in regard to the theory of the local origin of carcinoma of the breast.

I have used the three years' limit as a standard of time representing a permanent cure, because all writers upon malignant disease accept this period of time for the purpose of establishing some fixed rules in regard to the recurrence of malignant disease. I am well aware that carcinoma of the breast returns even when a patient has enjoyed an immunity for over three years. These cases are, however, rare, as they amount to scarcely 2 per cent. at present, and in order to establish some views in regard to the curability of carcinoma of the breast it is obvious that some fixed period must be adopted from which as a basis to argue. It is true that time is a relative term, and any other period beyond the three years' limit might be cited, but no duration of time to which the same objection might not be raised. The case of Dr. Pierson illustrates the fact that for our purpose three years' limit answers as well as twenty-five years.

The recurrence of carcinoma of the breast is influenced, *first*, by the period of time from the appearance of the growth to the date of the operation. I have searched very carefully through the literature of the subject to ascertain, if possible, to what extent the duration of the disease before operation influenced the question of recurrence. Statistics furnish us with no accurate data upon this point. In a study of my own cases bearing upon this subject I have found that in all the cases in group "A," which class represents a permanent cure for three years or more, that the tumors were removed on an average of six months from the date of their first recognition in the breast. It is also an interesting clinical fact that in nearly all the cases of permanent cure, the axillary glands were not invaded, or at least there was no microscopical proof of an invasion.

In all probability, within six months from the date of the first appearance of the induration in the breast in the cases belonging to group "A," the axillary glands were not infected; at all events the microscopical examination of the glands failed to show any changes. That it is possible for the glands to become infected within this period of time is well established. In other words, that the earlier the disease can be detected, the better the prognosis as regards any recurrence, and in a large majority of the cases the disease can be diagnosticated at a time before glandular infection has taken place; and that if the tumor can be removed within six months from its incipency and the axillary glands and fatty tissue be dissected out, and likewise the pectoral fascia and the peri-mammary fat and para-mammary areolar tissue, the prognosis will yield brilliant results not heretofore realized.

Great stress, therefore, should be placed upon the early recognition of the disease, and likewise upon the complete removal of the tumor, for the cases in group "A" demonstrate emphatically that recurrence can be usually prevented by carrying out these rules.

The recurrence of carcinoma of the breast is influenced, *second*, by the extent to which infiltration has taken place by any one or all of the three well-recognized ways of dissemina-

tion. When the tumor has existed long enough to show evidence of glandular enlargement, or integumentary infiltration, or metastatic deposit, the disease has been present for some time. If the breast and its adjacent structures are removed with the axillary glands and fatty tissue in the axilla there is still a prospect of success; but if metastatic deposits have occurred in the distant visceral organs there is hardly a tangible hope for recovery.

In regard to the first two ways of infection, if the area is circumscribed the radical operation may be successful; but if the case had become infected by the third way of dissemination, there is no opportunity offered by any surgical operation to save the patient. The question then is, if the infection has occurred within specific limitations by the first and second ways of dissemination—*i. e.*, by contiguous dissemination and by lymphatic infiltration—there is a prospect of cure offered by a radical operation. If, on the other hand, the infection has spread by the third way, which is by metastasis, there is no hope for a cure. It is a clinical fact worthy of attention, that of the cases in which secondary infection from the breast has occurred, nearly 90 per cent. of them invade the axilla, or, in other words, the disease has disseminated in nearly every case by a way that is amenable to treatment by surgical operation if taken in time. It is also a clinical fact of a startling character, that in cases where metastases have occurred, nearly 50 per cent. involve the lung or pleura, and it can be demonstrated that in the majority of cases the axillary involvement antedates the lung and pleura infection by several months, which points logically to an important fact that excision of the axillary glands with the fat in the axilla is an *imperative* step in the operative technique with a view to avoid recurrence of the growth after removal. In one case in group "B" a most extensive and dangerous dissection was necessary, and this patient has as yet no evidence of return. The glands deep in the axilla and those beneath the clavicle were all involved.

In another case the dissection was even more extensive as the pectoral muscle was removed and glands surrounding the axil-

lary and subclavian vessels were torn away from the vessels. In this case permission was given to remove the arm at the shoulder-joint if necessary to make the operation complete. Dissemination in this case was by the first and second ways and no recurrence ever followed this dangerous operation. Subsequently, however, metastasis occurred in the brain. Here complete operation prevented the further spread of the disease by the first and second ways of infection, but it did not prevent a metastasis, which is the third way of dissemination. Surgical interference can prevent recurrence because in 90 per cent. of the cases the return of the disease can be combated, or even prevented, by removal of the axillary glands and fatty tissue in addition to the complete removal of the breast.

The recurrence of carcinoma of the breast is influenced, *thirdly*, by the radical character of the operation itself.

No procrustean rule can be laid down in regard to the extent or character of the operation for the removal of carcinoma of the breast which would meet the exigencies in every case. A radical operation in one case would be an unjustifiable one in another case. For example, in one patient upon whom I operated it was necessary, besides removing the breast and all its subjacent tissue, and the axillary glands and fat, the pectoral fascia, and the pectoral muscle, to also excise the ribs, the removal of which exposes to view the pleural cavity. The ribs were involved in the carcinomatous infiltration, and were thin and eroded through the malignant ulcerative process. This is the first case I can find where the ribs were involved, and where in the course of the operation it became necessary to excise them.

The radical character of this operation would be no index to guide the surgeon in another case, and consequently a radical operation must be performed with certain limitations suited the special case. There is, however, a standard operation which is none too severe to meet the necessary conditions in every case. The uniform classical operation should include the entire breast gland, all the fatty areolar connective tissue in the vicinity, the integument over the circumscribed area of the tumor and as

much more as is necessary, leaving out of consideration altogether the question of flaps to cover the wound, and finally, the pectoral fascia.

Dr. Halsted has beautifully demonstrated that the pectoral fascia is involved in many cases of carcinoma of the breast, although to the naked eye, or to the sense of touch, this infiltration may not be apparent. I have been able to verify this opinion in several cases. I am aware that surgeons will dissent from this severe method of operating just described, on the ground that they can refer to cases where a less serious operation had been performed, and no return of the disease followed.

Any argument deduced from an individual case is unsound, and is often a source of error in estimating the radical character of an operation.

In the radical operation the death-rate is reported over three times as great where the complete operation is performed, in contrast to the incomplete; but these figures include cases of pre-antiseptic surgery, and are therefore misleading.

In my cases of carcinoma of the breast, if the case of hæmophilia is excluded, there was no death due to the operation. These operations were, as a rule, radical in the sense in which I have used the term, and instead of 7 per cent., or 14 per cent., or 23 per cent., there has not been a death due to the operation. I believe with every convenience at hand for performing the radical operation, and with antiseptic precautions in the higher use of the term, the operation is perfectly safe beyond the ordinary risks which attend a most trivial operation in which an anæsthetic is employed.

No patient should die from ordinary hemorrhage, or from septicæmia, or from any of the remote causes due to the operation.

The direct influence upon the recurrence of the tumor by the character of the operation is illustrated by the fact that 27 per cent. more of the cases of recurrence followed the incomplete operation as contrasted with the complete.

The question of mortality of the operation itself is one of importance, for it is obviously of no avail to remove completely a carcinoma of the breast and enucleate the axillary glands,

and tear out the axillary loose fatty tissue, if the patient's life is to be sacrificed in the performance of the operation itself. Let us for a moment investigate this problem, for its solution will throw a flood of light upon the question of recurrence of the disease after operation. After a careful study of the published mortality of the operation, I am convinced that it is the result of this investigation that has made surgeons too conservative. I am aware that the death-rate of the operation is very high, and I cannot account for this excessive mortality. For example, a reference to the published reports made by surgeons reveals the fact that the mortality of amputation of the breast, including both the complete and incomplete operations, was in Gross's cases about 10 per cent.; in Oldekop's cases, 9 per cent.; in Sir Joseph Lister's cases reported by Mr. Watson Cheyne, about 8 per cent.; in Butlin's cases, 7 per cent.; in Prof. Billroth's clinic, about 23 per cent.; in Prof. Fischer's clinic, 20 per cent.; in Prof. Esmarch's clinic, about 10 per cent.; in Prof. Küster's clinic about 14 per cent. In another list of operations, published by Billroth, the mortality is about 15 per cent. In a still later list of 68 cases performed by Billroth, there is a death-rate of about 6 per cent. In my own list of cases of amputation of the breast, the death-rate was 1.4 per cent. This is the lowest death-rate that has as yet been reported. If the one case of death which was due to continuous bleeding in a patient suffering from hæmophilia be excluded, as it can be with propriety, there is no mortality whatever connected with the operation in my series of 71 cases of amputation of the breast. I may add that in my list of 71 cases I have endeavored to perform the complete operation as far as was indicated, and the axillary space was opened in nearly all the cases; and in one case the ribs excised and the thoracic cavity opened.

Before finishing this most important part of our subject, I cannot refrain from entering a strong protest against Mr. Butlin's views in regard to partial amputations of the breast in cases of carcinoma of the gland. I have been deeply and profoundly impressed with a study of his book on malignant disease, but I cannot indorse his opinions in regard to incomplete

operations upon the breast for carcinoma. I am a strong advocate of always removing in every case, to which there is no exception, the entire breast with the pectoral fascia and the lymphatic glands as the minimum operation in the most insignificant scirrhus.

The operation in nearly all cases must extend beyond the limits of the breast and include a most radical one. In support of this view I can only add, that as a matter of clinical evidence the recurrences of the disease in my cases are much less frequent, and the mortality of the operation only 1.4 per cent., which is not more than would attend an amputation of the finger in pre-antiseptic days. In fact, there was no mortality if the case of hæmophilia be eliminated since it had no special bearing on this operation.

The last reason that I would adduce to strengthen the argument that the operations should be more radical in order to prevent recurrences, is the report of Küster, who submitted to careful microscopical analysis the glands removed in 117 cases of carcinoma of the breast, and in only two cases out of the 117 did he fail to find unmistakable evidences of carcinomatous infiltration. No sounder argument could be advanced than one based upon this report, and it is thus evident that not only the breast must be removed but also the axillary glands in order to minimize the dangers of recurrence of the disease. Mr. Heneage Gibbes has also verified this opinion in his excellent article on the formation of secondary growths in carcinoma. He has proved that carcinomatous infiltration is thus found in the axillary glands even when by other means the infiltration cannot be recognized.

The radical operation removes cancerous cells that form the foci for recurrences. These cancer-cells may be found outside the limits of the breast gland, lodged in the adjacent mammary region, whence they have been carried by the lymphatic current. I have several times found cancerous masses upon and in and under the pectoral fascia as well as in the neighboring muscles. These masses were examined microscopically and found to contain cancer-cells. Mere removal of the breast is inadequate to

reach the entire disease. In order to secure immunity from the disease in every case, it is necessary to adopt a radical operation as routine treatment in all cases. In a most valuable paper by Heidenhain, presented at the meeting of the German Congress of Surgeons in Berlin, 1889, he pointed out the fact that the ligaments of the breast are often surrounded by projections of the parenchyma of the gland and contain cancer-cells. This is true in regard to the so-named ligaments of Sir Astley Cooper as well as those which are retro-mammary and which bind the breast to the fascia. I have even found cancer-cells in the pectoral muscle, the adhesion of which to the posterior surface of the gland indicates the certain presence of cancerous emboli in the lymphatics of that muscle.

Gross was entirely right, some years ago, when he strongly urged the complete removal of the breast as a *sine qua non* to prevent recurrence. Mr. John Chiene even goes further than this, and takes a flap from the arm to cover the wound. The operation, in order to be radical, must be an extensive one. How seldom any surgeon completely removes the breast is tested by a method suggested by Mr. Harold J. Stiles, M.B., F.R.C.S.E., Assistant to the Professor of Surgery in the University of Edinburgh, Professor Chiene, and communicated by him from the Surgical Laboratory of the University of Edinburgh to the American Surgical Association in Washington. It is with great pleasure I make this communication, because it is a new and reliable method of testing the radical character of an operation and an operation never heretofore publicly brought to the attention of surgeons. I shall take the liberty of reading the description of the method as given by Mr. Stiles in his own manuscript.

“THE NITRIC ACID METHOD.

“1. *Wash the mamma in water to remove all traces of blood.* This is important, because after treatment with nitric acid the blood becomes blackened and difficult to remove, and therefore greatly obscures the appearances which the method brings out.

“2. *Submerge the whole organ in a 5 per cent. aqueous solution*

of *acidum nitricum*, *B. P.*, for about *ten minutes*—that is to say, during the time the surgeon is clearing out the axilla.

“3. Wash in plenty of running water for five minutes.

“4. Place in methylated spirit (undiluted) for two or three minutes.

“5. Examine the whole surface very carefully to ascertain:

“(a) Whether any part of the tumor itself be exposed upon the surface.

“(b) Whether any locally disseminated cancer foci be exposed upon the cut surface.

“(c) Whether breast tissue be exposed.

“The effect of the above method is to render all *carcinomatous* tissue and *parenchyma* dull and *opaque white*, due to coagulation of the albumin of the protoplasm of the cancer and epithelial cells.

“The *fibrous tissue of the stroma* is rendered *gelatinous, translucent, and homogeneous* in appearance, and somewhat India-rubber-like in consistence.

“The *fat* is *unaltered*.

“After examining the surface of the organ it should be cut into thick slices, and these are to be treated again in the same way.

“In this way the various normal and pathological constituents of the mamma can be readily and most satisfactorily studied.

“Cancer and parenchyma can at once be detected, if present, upon the surgeon's cut surface, and, since the examination can easily be completed before the time for suturing the wound, we have, in this method, a means which affords the surgeon a valuable aid in ascertaining the limits of the disease and of the organ.

“In two cases recently operated on by Professor Chiene, I was able to point out to him a speck of cancer, no larger than a pin's head, exposed upon the cut surface of the mamma. A corresponding point of the wound was searched, and in each case the remainder of the disease was discovered and removed. I possess microscopic preparations proving their cancerous nature.

"It is necessary to point out, however, that even although no locally disseminated foci may be discovered upon the surgeon's cut surface, the prognosis is not necessarily good, because, as we have already seen, the presence of lymphatics containing cancer-cells cannot be detected with the naked eye.

"I should remark that step No. 4, viz, washing with methylated spirit, is not essential, although it renders the appearances rather more distinct.

"For a subsequent more exhaustive study of the parts, I have been in the habit of replacing the slices in the nitric acid solution for a few hours, and subsequently washing for an hour or so. The specimen may then be placed in undiluted methylated spirit (which becomes brown, and should be renewed at the end of twenty-four hours), and the appearances are permanently retained.

"Excellent drawings may be made from specimens so prepared, and they afford the only illustrations I have seen in which accurate detail and differentiation have been brought out.

"In a microscopic investigation of tumors of the breast, we have, in the nitric acid method, a means which enables us to select exactly those portions of tissue which are most likely to illustrate special points, and in this way much time and labor is saved.

"Those slices, however, from which pieces are to be selected for microscopic examination must not be allowed to remain in the acid solution for more than a few minutes, as the acid renders the tissue too hard for section-cutting."

The recurrence of carcinoma of the breast is influenced—

Fourth, by the histological character of the carcinoma itself. This cause I believe to be most important in regard to the question of recurrence of the disease. The research into this subject has involved much labor, but the result has been most satisfactory in establishing some fixed laws regarding the return of carcinoma of the breast after excision. The microscopical examinations have been made, as the cases occurred, by Drs. Biggs, Dunham, and McAlpin, and the reputation of these men

is my guarantee as to the certainty of the diagnosis of carcinoma of the breast.

Before entering upon an analysis of these tumors, I desire to present some general facts in regard to the histology of tumors as a preface to the subject. In order to clearly comprehend the important questions bearing upon the recurrence of carcinoma of the breast after operation, it seems also to be pertinent to review some points in regard to the origin of tumors, among which may be conspicuously classed carcinoma. It makes no difference whether we accept the theory of the origin of tumors as propounded by Conheim, who believes that tumors develop by embryonic remains and that the neoplasm is the result of an excess of cells in the growing embryo, or whether we accept the older theories of tumor genesis, we are confronted with certain histological facts in the formation of every simple or compound tissue tumor.

We must appreciate in the higher sense, that while tumors and normal growths have a common origin in the cells of the tissues, and a common development in cell-segmentation, that there are certain characteristics which distinguish tumors from ordinary growths, and that among these marked features of tumor-growths may be mentioned their want of harmony in the economy, their absence of function, their lack of purpose, their total destruction of the organism in which they are found, and their failure of subordination to natural laws of growth. The reception accorded by the economy to a tumor is one altogether different from that accorded to inflammatory tissue. The tumor is considered as an independent entity, stealing its nutriment from the animal economy and maintaining itself from the organism by the intervention of lymph and vascular systems, and having no nervous connection with the organism.

We must recognize the tumor as an outgrowth of the tissue-cells which are found in the body, and we must further accept the fact that this cell-multiplication is asexual, and that the increase is by fission and cleavage of the protoplasm of the cells. Dr. Dunham, of the Carnegie laboratory, has prepared for me some slides showing most beautifully the segmentation process

in a fresh specimen of epithelioma recently taken from a patient now suffering from this disease. They are here for inspection to-day.

If, then, a tumor is considered as a growth derived from the same origin as repair-tissue, but with no proper function or purpose, it follows that the cells of tumors must have a wide difference, just as the cells of normal growth differ. It is this difference in the cell itself that marks the distinction between malignant and benign tumors. There are likewise differences between the cells of malignant tumors, and if it can be demonstrated that the clinical history of any case of carcinoma coincides with the special variety of cells, the recurrence of carcinoma of the breast after excision can be predicted with a tolerable degree of accuracy.

This cause of recurrence of carcinoma of the breast has received little, if any, attention by surgical writers. There has always been a general impression that the atrophic scirrhus, for example, was less malignant than the medullary carcinoma. The reasons for arriving at this conclusion have never been investigated from a purely histological and clinical point of view. I shall endeavor to demonstrate by a complete microscopical examination of my own cases, taken in connection with the clinical history extending over a period of three years, that the histological character of the tumor itself influences more than any other cause the recurrence of carcinoma of the breast. I shall also strive to prove that a reliable prognosis can be made from an examination of the nature of the histological elements which form the neoplasm. I have carefully prepared the clinical histories in each case, and then submitted each tumor for a complete microscopical examination. The result is that the tumors which show structures departing but slightly from the normal correspond in every case with the group of cases the clinical histories of which are favorable; because no return of the carcinoma has occurred in any case belonging to that group. The tumors that showed a great departure from the normal structure corresponded to the unfavorable clinical histories. In other words, the microscopical report of the tumors corresponded

precisely to the clinical histories. The more typical the structure, the better the prognosis; the more atypical the structure, the more unfavorable the prognosis. Arranging all the cases in four groups, and comparing the microscopical examination with the clinical histories, the recurrence and the non-recurrence of the disease in each case corresponded exactly. The plan of the arrangement of the groups will be explained in discussing this question from another point of view.

The result of the histological examination when compared with the clinical histories in this series of cases demonstrates that the more embryonic the structure of the tumor the greater the liability of recurrence. There seems to be a marked distinction, based upon the variety of the epithelial cells. An epithelioma derived from epithelium situated upon surfaces for mechanical protection, such as the skin, mucous membrane, etc., is less likely to recur than where the epithelioma takes its origin from the epithelium situated in the secreting glands, such as are found in the rectum, or from the epithelium which forms the true parenchymatous structure of a gland, such as the mammary gland. The history of epithelioma of the lip as compared with epithelioma of the breast, forcibly illustrates this law. The reason is very apparent, as Mr. Heneage Gibbes has demonstrated when he shows by microscopical examination that the carcinomatous cells lie in contact with the stroma. It is inferred that by amœboid movement these cells pass into the interfascicular lymph-spaces, from whence the lymphatic capillaries carry the cells into the nearest gland. This explains the frequency of recurrence of carcinoma in the pectoral and axillary glands and the metastases later on in the lungs and pleura. That recurrence takes place first in the neighboring glands is shown by the fact that in 128 autopsies of patients dying from carcinoma of the breast 90 per cent. of the cases had return of the disease in the axilla, and of the entire number 45 per cent. involved the lung and pleura and nearly 43 per cent. involved the liver. Primary carcinoma of the axilla, of the lung, of the pleura, or of the liver is so rare that it may be considered among the medical and surgical curiosities, whereas secondary

carcinoma is extremely common. Thus it is evident, to review the points under this fourth cause of recurrence, that epithelioma develops by asexual cell-proliferation, and that the more embryonic the cell is the more malignant the growth, and that the nearer the cell comes to the normal the less malignant the growth. It further follows that there is a marked difference between cells in repair-tissue, and that there is also a great difference in cells in tumor-growths, and that a prognosis of the malignancy of a tumor can be made by an examination of the character of the cells. Finally, the clinical histories corresponded with the histological examinations, and that this cause of recurrence, due to the special development of the cells, has been proved beyond a doubt, not by general statement but by directly comparing in each case the precise clinical history with the histological examination. We are thus enabled to demonstrate that recurrence of carcinoma of the breast actually corresponds to the character of the cells which form the carcinoma, and that this proof rests upon a thorough investigation of the patients whose clinical histories have been accurately kept for many years and taken in connection with the microscopical examination of the tumors.

The recurrence of carcinoma of the breast is influenced, *fifth*, by the appearance simultaneously of carcinoma in both breasts. Fortunately this condition only exists in about 5 per cent. of the cases. In cases which have come under my observation of double carcinoma of the mammæ, one has died within a year after removal of both breasts, and the second patient is still alive and well. It is now over three years since the removal of both the mammary glands.

The appearance of double carcinoma makes the prospect of recurrence greater, owing to the more extensive infiltration. In double carcinoma of the breast the secondary deposits are most likely to occur. These infiltrations and metastases are found very early in the history of the case.

The recurrence of carcinoma of the breast is influenced, *sixth*, by the personal factors of the individual, such as age, sex, mar-

riage, fecundity, sterility, traumatism, heredity, menstruation, metastasis, mental condition, locality, race, nativity, etc.

In order to draw any conclusions from the personal factors as to recurrence of carcinoma after removal, it must be assumed that any laws which operate to develop carcinoma primarily have not entirely lost their influence in bringing about a recurrence. The capability is not always removed with the local infection. This view is in perfect harmony with the constitutional theory of carcinoma and can be easily reconciled to the theory of local origin of cancer—a theory in which I am a firm believer.

That carcinoma may be present in the body in more than one place at the same time, and a common cause independent of auto-infection underlying the malady, has been proven in many cases.

Age has an indirect influence upon recurrence or metastasis, since it has a marked effect upon the primary growth. Gross has pointed out the fact that 82 per cent. of the cases of primary carcinoma of the breast develop after the fortieth year, and that the average is the forty-eighth year. Carcinoma of the breast is seldom, if ever, present in early life; although carcinoma in general has been frequently observed before the fifth year. In an analysis of 194 cases only 3 cases appeared after the seventy-first year, and only 1 after the seventy-sixth year. The tendency to the development of carcinoma of the breast is declining after sixty years; the conditions are also unfavorable for recurrences or metastases. It is an interesting fact that the maximum frequency of carcinoma appears ten years earlier in the female. In my list of all the cases permanently cured, all are under fifty years, except one; and notably, in all the cases in which there was a return followed by death, the patients were over fifty years of age. In other words, there seems to be less malignancy in carcinoma affecting the breast in the early stages of obsolescence of the gland than when the gland has fully completed its degenerative changes. Age, therefore, has marked influence in regard to recurrence, for the older the patient is, within certain limitations, the more malignant the

carcinoma appears. The nearer the gland is to a healthy functional activity the less likely is it to assume malignancy.

Sex has an indirect influence upon the recurrence of carcinoma of the breast, since the disease exists in the male in the proportion of one to every one hundred cases in the female. In my list there was only one case in the male sex.

Metastases occur in over six per cent. of the cases of breast carcinoma in those organs in the female that are absent in the male, and metastases are seldom, if ever, found in the corresponding organs in the male. I have observed six additional cases of carcinoma of the breast in the male besides the one already mentioned. These cases were treated by the late Dr. James R. Wood, and in no case belonging to his list did recurrence occur as far as I have been able to ascertain.

Marriage without doubt has a direct influence upon primary carcinoma of the breast, since 80 per cent. of the cases are found among married women. This would leave 20 per cent. to represent the unmarried class. The same law, therefore, which operates to cause carcinoma in one breast incident to marriage will not altogether lose its force in causing a further extension of the disease in the opposite breast, or by dissemination by the first way of infection in the cicatricial tissue. In my list of permanent cures, all the patients except one were married.

Fecundity seems to affect the frequency of carcinoma of the breast. Mr. Thomas Bryant, in his excellent book upon *Carcinoma of the Breast*, has pointed out the interesting clinical fact that 74 per cent. of the women were prolific, while only 26 per cent. were sterile. To quote from his book, Mr. Bryant states that "a large proportion of the prolific women were so to an extreme degree, ten or more children to one mother being a common note to find recorded."

In my list I find that all the married patients had children, except one. In other words, there was only one patient who was married and who was sterile. These patients, however, were not prolific to an extreme degree as in Mr. Bryant's cases. The average was three children, instead of ten or more as in Mr. Bryant's cases.

Traumatism has a direct influence on the development of carcinoma of the breast in about 13 per cent. of the cases, according to some writers. In the male, traumatism has been assigned as the cause in nearly 50 per cent. I am certain that if friction, irritation, and mechanical stretching of the scar after removal of the breast can be classed under the head of traumatism, a very large proportion of the cases of recurrence are due to this cause, the prevention of which is possible in many cases.

If wearing unsuitable corsets can in any way be assigned as a cause to develop carcinoma in a woman in whom a predisposition exists, certainly this would be a most potent factor in the etiology of recurrence. A soft pad should always be worn in contact with cicatricial tissue following excision of the breast, in order to obviate one of the causes of the recurrence of carcinoma.

Thus it is evident that if traumatism will act as an exciting cause to develop carcinoma in the breast, it will operate in the same way, under given conditions, to cause recurrence or metastases in a patient favorably predisposed.

The recurrence of the disease in the scar can be largely prevented by the exercise of care in instructing the patient how to treat the tissues thus formed after the removal of the breast. Some idea of the importance of mechanically protecting the scar after removal of the breast can be formed by the knowledge of the clinical fact that a study of the cases of recurrence of carcinoma of the breast shows it to occur in "nearly every instance"—according to Butlin—"under or close to the scar." Von Winiwarter has also demonstrated that in Billroth's cases the recurrences originated in the scar-tissues. This idea impressed the late renowned Langenbeck to such an extent that I remember his having suggested in his clinic the dressing of the wound with the patient's arm placed at right angles to the trunk, in order that the scar-tissue might form without contraction. In this way the subsequent moving of the arm might not cause stretching of the cicatricial tissue, and thus give rise to a continual irritation in a variety of tissue so prone to be the starting-

point of recurrent carcinoma. In point of fact, the cicatricial tissue usually forms the new focus that appears after removal of the breast.

I have been in the habit of dissecting away the scar when it is found to be inflamed or when it seems to be irritated by stretching. This I believe to be a practice that should be adopted in all cases where the scar is irritated, even years after the original removal of the breast. This procedure will certainly remove a potent cause of recurrence of carcinoma after excision of the breast.

Mastitis accounts for nearly 30 per cent. of cases of carcinoma of the gland. If this irritation is sufficient to develop the disease in the breast of a patient in whom a predisposition exists, a comparable irritation, like a low grade of inflammation in young connective tissue, certainly would have a corresponding influence.

In one patient upon whom I have operated for carcinoma of the breast—in the case of the wife of a well-known physician—traumatism in the form of a fall upon the breast where the patient struck upon the edge of the bed, developed a carcinoma in one gland, while the other breast, which had been previously the seat of mastitis leading to abscess-formation, escaped. In other words, in this case traumatism seemed to have been a more potent factor in causing carcinoma in a breast than mastitis; for the breast exposed to traumatism developed carcinoma, while the breast which was the former seat of an abscess has shown no tendency to give rise to the disease, although the evidences of an old abscess are still apparent in the remaining breast.

In my list of cases studied with reference to this point, I find that mastitis is quite common; but I also find that in the most malignant group traumatism stands out as a most prominent etiological factor—more so than mastitis.

Heredity also may be assigned as a factor in developing secondary growth in 12 per cent. of the cases. A study of the cases of carcinoma of the breast will demonstrate the fact that a larger number of recurrences and metastases will be found in

those cases of carcinoma of the breast in which an hereditary influence is present.

Metastasis has a marked influence, because its presence shows that the disease has been extensively disseminated throughout the system, and, therefore, recurrences are most likely to ensue after the removal of the primary growth.

The *mental condition* has also an influence upon recurrence, because an anxious, nervous, restless, and irritable frame of mind predisposes by loss of sleep, imperfect digestion, etc., to depreciate the normal condition of health and thus devitalize the tissues, which renders the soil favorable for recurrence of malignant growths in the same manner that it predisposes toward the development of the primary growth.

The *locality of carcinoma* has a marked influence upon the recurrence after its removal. Carcinoma is prevalent in the New England States and on the Southern Pacific Coast, in the central part of Michigan and the southern part of Wisconsin. Dr. Billings has pointed out the interesting fact that in "any given locality a large proportion of cancer indicates that the locality is healthful and a long-settled one, and has a large proportion of inhabitants of an advanced age."

In my list of permanent cures all the patients of carcinoma of the breast lived in and about New York, or at least within a radius of fifty miles from the city, with only one exception, and this patient came from New England.

Race has a marked effect upon the development of carcinoma of the breast, and hence the law operates in regard to the recurrence, or metastases, or multiplicity of growths. There is a marked difference between the white and colored race, as regards carcinoma. For example, among the whites the proportion of deaths from carcinoma per 100,000 is about 20 per cent., and for the colored race about 5 per cent.

Carcinoma, irrespective of age, is more than twice as prevalent among the whites than among the blacks. It is also a disease rarely found among the Indians, or the uncivilized inhabitants of the islands of the Pacific. In my list there were only two cases among the colored race.

Nativity seems also to influence the development of carcinoma, and also the recurrence. The Germans are more liable to carcinoma than the Irish, and the Irish more than the native whites. The idea can be expressed more tersely by saying that carcinoma is found more than twice as frequently among the foreign-born population than it is among the native-born of the United States.

The negro seems to enjoy an immunity from carcinoma to a certain extent, either as a primary growth or as a secondary deposit, or as metastases in distant organs from the breast focus. Native-born Americans are less liable to the disease, with its recurrences or its metastases, than the Irish or the Germans.

I shall now condense my operative work in carcinoma of the breast, in which I have for over ten years carefully followed up all the cases, in only two of which have I the histories to record as unknown.

The conclusion to which I have arrived from a careful study of these cases, in regard to the question of recurrence of carcinoma of the breast after removal, will be considered. In the first place, I have complete notes of 105 cases of tumors of the female breast which have come under my personal care. I have incomplete notes of many other unpublished cases that I have treated in addition to the 105; but, as the histories are so defective as regards the union of the clinical history with the microscopical examination, I shall exclude them altogether in the summary.

In the 105 cases of tumors of the breast never before published, there are 34 cases which must be eliminated, because among the 105 cases there are specimens of adeno-fibromata, sarcomata, cystic tumors, galactoceles, syphilitic mastitis, and other varieties which do not belong to carcinoma. There are also a few cases of carcinoma of the breast in which the disease had extended so far as to render any operative interference unjustifiable, and also there are a few cases in which the patients themselves declined any operation. Deducting these cases from the total number, there are left 71 cases of amputations of the breast.

The cases of carcinoma of the breast I have arranged into four separate groups:

In Group A are found cases in which the patients are permanently cured, or where the patients have reached the three years' standard of time without any evidences of return.

In Group B are found cases in which the patients have not yet quite reached the three years' limit of time, and, therefore, according to the standard mentioned, cannot be said to be permanently cured.

In Group C are found cases in which the patients have been operated upon and in whom a recurrence of the disease in the scar or in the axillary gland has taken place, followed by death.

In Group D are found cases in which the patients have been operated upon, and in whom metastases have occurred in visceral organs, followed by death.

I have before me on the table the history of each case and a microscopical slide of the tumor, with a written opinion from one of the three well-known microscopists already mentioned. I have also appended the names of the physicians who were present at each operation. The tumors are preserved in alcohol and are in my private collection of pathological specimens in the museum of the Carnegie Laboratory.

These histories, the microscopical slides, and the tumors themselves, are at the disposal of anyone who may be specially interested in this subject.

In regard to the operative cases, I have performed amputation of the breast seventy-one times, and in nearly every case opened the axilla and removed the glands. In one case the ribs were excised, in order to remove all the neoplasm. In this series of seventy-one consecutive cases one patient died from the immediate effects of the operation. This patient suffered from hæmophilia and bled to death, in spite of everything that could be done to prevent the constant hemorrhage. Including this case of death, the mortality of the operation is 1.4 per cent.

If this one death occurring in the patient who suffered from hæmophilia be eliminated, a death that would have resulted in

the event of any other serious or even trivial operation, and a death that can be with propriety excluded as far as bearing upon this special operation is concerned, there is an unbroken series of seventy consecutive cases without a death. In addition to the reduction of the mortality from as high as 23 per cent., recorded by Billroth, to a cipher, it can be also said that there was no case of pyæmia, septicæmia, erysipelas, or abscess.

Besides the question of mortality, the question of permanent cures effected by the operation is one to which great interest is attached.

In the list of seventy-one cases of amputation of the breast, a number must be eliminated in estimating the percentage of permanent cures. This is necessary because some of the tumors were of other varieties of malignant disease, and while this would not effect the question of mortality in reference to the operation of amputation of the breast, it would effect materially the question of cures beyond three years in pure carcinoma.

In the thirty-three cases of pure carcinoma of the breast in which the clinical histories and the microscopical examinations are complete, there were eight permanent cures of over three years' limit of time. Deducting the two cases in which the histories are unknown, the result is over 25 per cent. of permanent cures beyond the three years' limit of time.

It is fair to assume that in Group B, where the patients have not quite reached the three years' limit, that there will be some who in a very short time can be classed in Group A of permanent cures. This would bring the percentage of cures up to nearly 30 per cent., if not over 30 per cent.

Thus a study of my seventy-one consecutive cases demonstrates the fact that the mortality has been reduced from 23 per cent., as published by Billroth, to 1.4 per cent., or, if the case of hæmophilia be excluded, from 23 per cent. to zero.

The percentage of permanent cures from 15 per cent., which is the best result, and published by Mr. Banks, to nearly double, or 30 per cent.

Finally, I believe this great reduction in the mortality of the operation will have a marked effect upon the radical character

of the operation in the future. As a natural sequence the percentage of permanent cures will be increased. I feel justified, in view of these facts, to prophesy that with early and radical operations the recurrence of carcinoma of the breast after removal of the gland will be, comparatively speaking, of rare occurrence. I feel confident that with the early recognition of the disease, and with complete operation together with the improved methods in the technique, amputation of the breast for carcinoma of that gland will yield results more brilliant and startling than the most sanguine surgeon could imagine.

The high death-rate in the operation has been largely due to causes which aseptic surgery can prevent, the frequent recurrences to causes due to delayed and incomplete operations. In some cases the returns are due to the character of the growth.

A new era is about to dawn in regard to this dark night of surgery, and patients who have hitherto been doomed to a certain death can be in the future rescued by the application of fixed and well-established principles which have been either never understood or overlooked. Surgery will thus prolong life and mitigate suffering. It will even save life in cases of carcinoma of the breast, a disease which in the past has blighted so many homes, but in the future will be deprived of its malign influence through the advances made by scientific surgery.





